

**CLAIM AMENDMENTS**

1-24. (new): (canceled)

25. (new): A pharmaceutical composition for parenteral administration, comprising particulate delivery vehicles having associated therewith at least a first antineoplastic agent and a second antineoplastic agent, wherein said first and second agents are in a mole ratio which exhibits a non-antagonistic cytotoxic or cytostatic effect and wherein said first and second agents are associated with the delivery vehicles to maintain a non-antagonistic ratio in the blood on administration.

26. (new): The composition of claim 25 wherein said delivery vehicles are 4 to 6,000 nm in diameter.

27. (new): The composition of claim 25 wherein said delivery vehicles have a mean diameter of between 4.5 and 500 nm.

28. (new): The composition of claim 27 wherein said vehicles have a mean diameter of less than 250 nm.

29. (new): The composition of claim 25 wherein said delivery vehicles are from 4 $\mu$ m to 50 $\mu$ m in diameter.

30. (new): The composition of claim 25 wherein said delivery vehicles comprise liposomes.

31. (new): The composition of claim 25 wherein said first and second agents are co-encapsulated.

32. (new): The composition of claim 25 wherein said mole ratio of the first agent to the second agent exhibits a non-antagonistic cytotoxic or cytostatic effect to relevant cells in culture

over at least 5% of the concentration range where >1% of the cells are affected in an *in vitro* assay for said cytotoxic or cytostatic effect.

33. (new): The composition of claim 32 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 10-90% of the cells are affected in said *in vitro* assay.

34. (new): The composition of claim 33 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 20-80% of the cells are affected in said *in vitro* assay.

35. (new): The composition of claim 34 wherein said non-antagonistic effect is exhibited over at least 20% of the concentration range such that 20-80% of the cells are affected in said *in vitro* assay.

36. (new): The composition of claim 25 which, when administered to a subject, provides a therapeutic activity greater than that which is obtained when said agents are administered in the same ratio but not associated with delivery vehicles.

37. (new): The composition of claim 25 wherein at least one of the agents is selected from the group consisting of a DNA damaging agent, a DNA repair inhibitor, a topoisomerase I inhibitor, a topoisomerase II inhibitor, a cell checkpoint inhibitor, a CDK inhibitor, a receptor tyrosine kinase inhibitor, a cytotoxic agent, an apoptosis inducing agent, an antimetabolite, a cell cycle control inhibitor, a therapeutic lipid, a telomerase inhibitor, an anti-angiogenic agent, a mitochondrial poison, a signal transduction inhibitor and an immunoagent.

38. (new): The composition of claim 37 wherein the first agent is a cytotoxic agent and the second agent is a cell-cycle inhibitor, or wherein the first agent is a DNA damaging agent and the second agent is a DNA repair inhibitor, or wherein the first agent is a topoisomerase I inhibitor and the second agent is a S/G<sub>2</sub> - or a G<sub>2</sub>/M- checkpoint inhibitor, or

wherein the first agent is a G1/S checkpoint inhibitor or a cyclin-dependent kinase inhibitor and the second agent is a G2/M checkpoint inhibitor, or

wherein the first agent is a receptor kinase inhibitor and the second agent is a cytotoxic agent, or

wherein the first agent is an apoptosis-inducing agent and the second agent is a cytotoxic agent, or

wherein the first agent is an apoptosis-inducing agent and the second agent is a cell-cycle control agent, or

wherein the first agent is a telomerase inhibitor and the second agent is a cell-cycle control inhibitor, or

wherein the first and second agents are antimetabolites, or

wherein the first and second agents are cytotoxic agents, or

wherein the first agent is a therapeutic lipid and the second agent is a cytotoxic agent, or

wherein the first agent is a topoisomerase I inhibitor and the second agent is a DNA repair inhibitor, or

wherein the apoptosis-inducing agent is a serine-containing lipid.

39. (new): The composition of claim 38

wherein the first agent is irinotecan and the second agent is 5-FU or FUDR, or

wherein the first agent is cisplatin (or carboplatin) and the second agent is 5-FU or FUDR, or

wherein the first agent is idarubicin and the second agent is AraC or FUDR, or

wherein the first agent is oxaliplatin and the second agent is 5-FU or FUDR, or

wherein the first agent is irinotecan and the second agent is cisplatin (or carboplatin), or

wherein the first agent is gemcitabine and the second agent is cisplatin (or carboplatin), or

wherein the first agent is methotrexate and the second agent is 5-FU or FUDR, or

wherein the first agent is paclitaxel and the second agent is cisplatin (or carboplatin), or

wherein the first agent is etoposide and the second agent is cisplatin (or carboplatin), or

wherein the first agent is docetaxel or paclitaxel and the second agent is doxorubicin, or

wherein the first agent is doxorubicin and the second agent is vinorelbine, or

wherein the first agent is carboplatin and the second agent is vinorelbine, or

wherein the first agent is 5-FU or FUDR and the second agent is gemcitabine.

40. (new): The composition of claim 39 wherein the first agent is irinotecan and the second agent is 5-FU or FUDR or  
wherein the first agent is cisplatin (or carboplatin) and the second agent is 5-FU or FUDR.

41. (new): A method to prepare a composition of claim 25, which method comprises  
a) determining in a relevant cell culture assay for cytotoxic or cytostatic activity a mole ratio of said first and  
second agent which is non-antagonistic over at least 5% of the concentration range over which greater than 1% of cells are affected by said ratio of agents, and  
b) encapsulating with said delivery vehicles a mole ratio of agents determined to be non-antagonistic in step a).

42. (new): The method of claim 41 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 10 - 90% of the cells are affected in said in vitro assay.

43. (new): The method of claim 42 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 20 - 80% of the cells are affected in said in vitro assay.

44. (new): The method of claim 43 wherein said synergistic effect is exhibited over at least 20% of the concentration range such that 20 - 80% of the cells are affected in said in vitro assay.

45. (new): The method of claim 41, wherein said determining employs testing at least one ratio of said agents at a multiplicity of concentrations and applying an algorithm to calculate a synergistic, additive, or antagonistic effect for said ratio over a range of concentrations.

46. (new): The method of claim 45 which employs testing a multiplicity of ratios, and wherein said algorithm is the Chou-Talalay median effect method.

47. (new): The method of claim 41 wherein at least one of the agents is selected from the group consisting of a DNA damaging agent, a DNA repair inhibitor, a topoisomerase I inhibitor, a topoisomerase II inhibitor, a checkpoint inhibitor, a CDK inhibitor, a receptor tyrosine kinase inhibitor, a cytotoxic agent, an apoptosis inducing agent, an antimetabolite, a cell cycle control inhibitor, a therapeutic lipid, a telomerase inhibitor, an anti-angiogenic agent, a mitochondrial poison, a signal transduction inhibitor and an immunoagent.

48. (new): The method of claim 47 wherein the first agent is a cytotoxic agent and the second agent is a cell-cycle inhibitor, or wherein the first agent is a DNA damaging agent and the second agent is a DNA repair inhibitor, or wherein the first agent is a topoisomerase I inhibitor and the second agent is a S/G<sub>2</sub> - or a G<sub>2</sub> /M- checkpoint inhibitor, or

wherein the first agent is a G1/S checkpoint inhibitor or a cyclin-dependent kinase inhibitor and the second agent is a G2 /M checkpoint inhibitor, or

wherein the first agent is a receptor kinase inhibitor and the second agent is a cytotoxic agent, or

wherein the first agent is an apoptosis-inducing agent and the second agent is a cytotoxic agent, or

wherein the first agent is an apoptosis-inducing agent and the second agent is a cell-cycle control agent, or

wherein the first agent is a telomerase inhibitor and the second agent is a cell-cycle control inhibitor, or

wherein the first and second agents are antimetabolites, or

wherein the first and second agents are cytotoxic agents, or

wherein the first agent is a therapeutic lipid and the second agent is a cytotoxic agent, or

wherein the first agent is a topoisomerase I inhibitor and the second agent is a DNA repair inhibitor, or

wherein the apoptosis-inducing agent is a serine-containing lipid.

49. The method of claim 48 wherein the first agent is irinotecan and the second agent is 5-FU or FUDR, or

wherein the first agent is cisplatin and the second agent is 5-FU or FUDR, or

wherein the first agent is idarubicin and the second agent is AraC or

wherein the first agent is oxaliplatin and the second agent is 5-FU or FUDR, or

wherein the first agent is irinotecan and the second agent is cisplatin (or carboplatin), or

wherein the first agent is gemcitabine and the second agent is cisplatin (or carboplatin), or

wherein the first agent is methotrexate and the second agent is 5-FU or FUDR, or

wherein the first agent is paclitaxel and the second agent is cisplatin (or carboplatin), or

wherein the first agent is etoposide and the second agent is cisplatin (or carboplatin), or

wherein the first agent is docetaxel or paclitaxel and the second agent is doxorubicin, or

wherein the first agent is adriamycin and the second agent is vinorelbine, or

wherein the first agent is carboplatin and the second agent is vinorelbine, or

wherein the first agent is 5-FU or FUDR and the second agent is gemcitabine.

50. (new): The method of claim 49 wherein the first agent is irinotecan and the second agent is 5-FU or FUDR, or wherein the first agent is cisplatin and the second agent is 5-FU or FUDR.

51. (new): A method to treat a disease condition in a subject which method comprises administering to the subject an effective amount of the composition of claim 25.

52. (new): The method of claim 51 wherein the subject is a human.

53. (new): The method of claim 51 wherein the subject is a non-human mammal or avian.